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REVIEW ARTICLE

Evaluation of the efficacy of injection of platelet-rich plasma for the management of "Peyronie's disease" and erectile dysfunction

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Abstract:

Background: This study evaluates and determines the therapeutic effects of platelet-rich plasma injection for the management of Peyronie's disease and erectile dysfunction.

Patients & Methods: From March 2021 until March 2022, a prospective study was conducted on 50 patients with Peyronie's disease, erectile dysfunction, and penile curvature less than 60 degrees (mild to moderate penile curvature). All participants were subjected to 8 repeated injections of PRP weekly in the dominant penile plaque, with follow-up over 6 months of collected data that included orientation of curvature, injection technique, and the results in both quantitative (i.e., curvature estimations) and qualitative (erectile state and pain during intercourse) forms and complications.

Results: 50 male patients with follow-up in pre- and post-injection regimes over periods of 2, 4, and 6 months; the results were collected. Only minor complications, i.e., mild penile swelling, bruising, edema, and allergy; important decrease in penile curvature comparable to baseline without noticeable worsening of curvature plaque in subsequent evaluations. Improvement in pain during sex (visual analog score) increased from 4 to 8. No significant improvement in ED compared to baseline (IIEF-5 score)

Conclusion: PRP in treatment for Peyronie's disease is safe, with unremarkable adverse effects and significant improvement in penile deformation. It is better for this therapeutic modality to be initiated in the early, i.e., active, phase of the disease since it is easy and well tolerated.

Keywords: Platelet-rich plasma, Peyronie's disease, erectile dysfunction, penile curvature, minimally invasive treatment.

Introduction

Peyronie disease (PD) is a benign, acquired condition pathologically characterized by exaggerated inflammation and an increase in the collagen composition, leading to fibrosis (scarring) within the tunica albuginea (TA) of the corpora cavernosum of the penis, causing penile curvature, decreased length or girth, or pain with intercourse (1). PD occurs in 5% to 8% of men. Usually occurs from the fifth decade but can occur at any age (2).

It is clinically characterized by 2 stages (acute PD) lasting between 6 and 12 months as scars form, causing a curve or change in penile shape with pain in an erection or flaccid state. (Chronic PD) scar tissue was stable, and there was no longer any change in penile deformity, distress in vaginal penetration, or erectile dysfunction (ED) (3).

The exact pathogenesis is not fully understood; PD is an abnormal wound healing (4) initiated by injuries that can occur during sex (such as bending the penis during penetration or pressure from a partner's pubic bone), sports activity, or following an accident. Systemic diseases, i.e., diabetes mellitus (DM), hyperlipidemia, hypertension, and ischemic heart disease, may play a role in the pathogenesis of this disease (5). A "modified Kelami classification" was used to classify penile deformities as follows:

Stage 1 patients with deformities without curvature (notching, hourglass, and swan neck deformities)

Stage 2: mild curvature (deformity angle ≤ 30 degrees)

Stage 3 moderate penile curvature (deformity angle between 31 and 60 degrees)

Stage 4: severe penile curvature (more than 60 degrees) (6).

In the management of PD in its stable phase, a distinction is made between oral pharmacological and intralesional drug injections (such as interferon alfa-2b, verapamil, and hyaluronic acid) (7), and the new modalities are regenerative extracorporeal shock wave therapy, intracavernous stem cell therapy (SCT), and platelet-rich plasma (PRP) injections, while surgical approaches are reserved for severe penile curvature that precludes sexual intercourse (8). Platelet-rich plasma is an autologous biological therapy containing five times the concentration of platelets comparable to whole blood. This therapy

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contains abundant growth factors like platelet-derived growth factor, fibroblast growth factor, epidermal growth factor, transforming growth factor b, vascular endothelial growth factor, and insulin-like growth factor. All are involved in complicated healing processes, especially neoangiogenesis, anti-inflammatory and antioxidant effects, and stimulated cellular growth. Recruitment of immune cells leads to resolution of plaque-related symptoms and limited plaque growth (9). In this study we evaluated the validation and the safety of PRP injections in the treatment of Peyronie's disease regarding improvement in penile contracture, sexual satisfaction, and erectile dysfunction.

Patients and Method

From March 2021 until March 2022, a prospective study on 50 patients with PD and ED enrolled in this study after giving informed consent.

Inclusion criteria: patients didn't receive any treatment for their PD previously; stable symptomatic PD (stable plaque older than 6 months); and penile curvature below 60 degrees either in the dorsal, lateral, or dorsolateral plane (mild to moderate PD).

Exclusion criteria included curvature of the penis more than 60 degrees (severe PD), history of receiving oral or injectional therapy for the PD, history of priapism, and calcified plaque that precludes proper administration of PRP. By utilizing a protractor (medical goniometer), we estimate the degree of penile angulation, which is the distance of the penile glans from the pubic line. This can be done either by self-photography of an erection (at home) or by inducing an erection by intracavernous instillation of a vasoactive therapy like trimix. Two photos are taken: one superior to see the right or left angle and one in the sagittal plane (superior or inferior). Pain during intercourse was evaluated by use of a conventional 11-point pain scale (pain intensity visual analog scale: VAS(10)), and erectile dysfunction (ED) was evaluated by use of the IIEF questionnaire (11).

Our patients were subjected to an 8-week cycle of weekly intraplaque injections under local anesthesia. They were injected with 5 ml of PRP by Doppler ultrasound guidance in intra- and peri-plaque at the level of the tunica albuginea of the corpora cavernosa on a detumescent penis with a 23 g × 32 mm needle. The injection site was pressed to prevent bruising, and he was kept under observation for an hour before he went home. Follow-up for our patients was 2 months after the end of therapy, then at 4 and 6 months. Evaluation of our measurements during follow-up, including plaque size (millimeters) assisted by duplex Doppler ultrasonography; degree of penile curvature; erectile state by using the International Index of Erectile Function (IIEF-5) score; pain during intercourse with sexual satisfaction, which was measured by utilizing a visual analog scale (VAS) from 0 to 10, where 0 represented "not satisfied" and 10 represented "satisfied"; and complications

Result

Gathering of our clinical data for this study shows a main age of 55 years (average 40-60 years), as in Fig. (1). All patients had a stable phase of PD (plaque more than 6 months) with one palpable plaque on the shaft at physical examination with a mean plaque size of 12 mm (average 8–30 mm); the main penile curvature was 35° (range 15°–45°) as in Fig. 2, with 23 (45%) of plaques geographically oriented to the left, 20 (40%) to the right, and 7 (15%) dorsally as in Fig. 3. The main IIEF-5 score was 20 (average = 0–25), with mild to moderate erectile dysfunction (IIEF score < 21) present in 27 patients in our study (54%). The main VAS score was 4 (average 2–10). No major complication was reported except that 2 patients had mild pain and bruising.

Mean follow-up after the last post-injection was 2, 4, and 6 months.

Fig :-(1) Age distribution

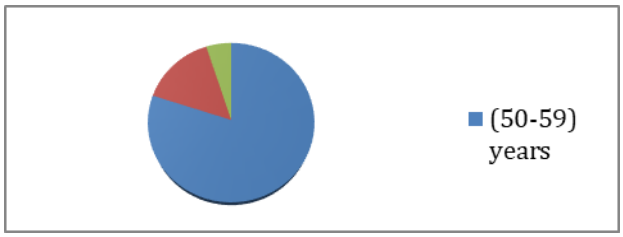


Fig :-(2) degree of penile curvature

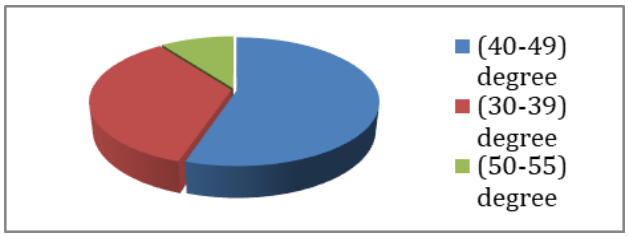


Fig :-(3) Orientation of penile curvature (%)

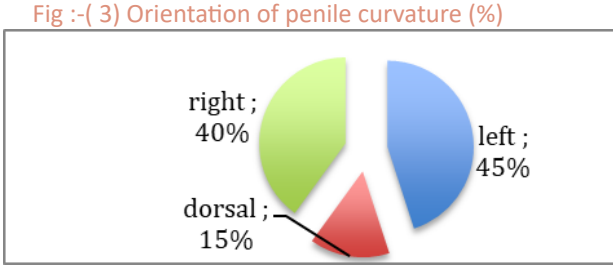


Table (1) demographic and pretreatment clinical data

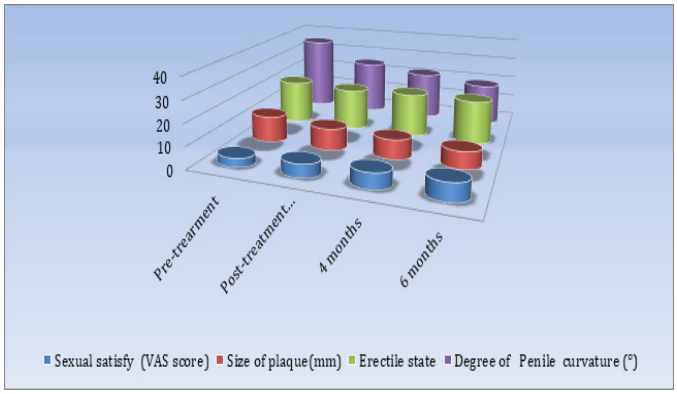
Baseline parameter	Main	Range
Age (y)	55	40-60
Plaque dimension (mm)	12	8-30
Penile curvature	35	15-45
IIEF-5 (score)	21	11-25
Penile pain During intercourse VAS (score)	4	(2-10)

Table (2) shows comparable results from pre- and post-injection follow-up. Considerable improvement was seen in the degree of penile contracture (pretreatment = 35° range (15-45°); after treatment, 25, 22, and 19 at follow-ups in 2, 4, and 6 months, respectively). No remarkable improvement in erectile dysfunction was seen in our patient as per the "IIEF-5 score" (before therapy, 20 {11–25}; after therapy, 20 [15–25]). Improvement in sexual satisfaction was noticed, i.e., the "VAS score" (before therapy, 4 {2–10}; after therapy, 8 {2–10}). Increases in penile size from baseline were reported in 4 patients (8%). Comparing our measurements at 2, 4, and 6 months shows in Fig:-(4)

Table (2) Clinical data after 8 intra-plaque treatment by platelet rich-plasma

Parameter	Post-injections (2months)	(4 months)	(6 months)
Degree of Penile curvature (°)	25	22	19
Sexual satisfy (VAS score)	6	7	8
Size of plaque (millimeters)	10	9	8
Erectile state (IIEF-5 score)	19	20	20

Fig: - (4) pre- and post-treatment follow up



Discussion

Usage of PRP has affected all medical fields, including hematology, rheumatology, dermatology (as in alopecia, acne, and burns), maxillofacial surgery, and orthopedics, where it received approval from the Food and Drug Administration (FDA) for bone transplantation. (12) PRP in the treatment of Peyronie's disease is safe; no major adverse effects or complications were observed (13). PD is generally found in men in the fifth decade of their life, where significant correlations have been observed between PD and age in many articles, as in Lindsay and Rhoden } **(14),** as well as in our study. The demographic orientation of penile deformity most commonly was the dorsal and lateral curvatures in our study, which corresponds to Brock et al. (1997) and Usta et al. (2004) (15). Left-sided orientation is more frequent than the right-sided orientation in our study (as in Fig. :-(3). Since the tunica albuginea is thicker on the dorsal aspect because of the abundant amount of collagen bundles, while it is thinner at the 3 and 9 o'clock positions, that explains why patients with lateral bending (curve) had milder abnormalities than those with dorsal bending, who had severe abnormalities. The therapeutic modalities of Peyronie's disease vary from oral medication treatments (analgesia, antioxidants, and pro-erectile drugs) in the early phase of the disease to more invasive intra-plaque injections or mechanical (traction and vacuum therapy) or surgical management like "penile plication," plate "excision/ incision," and grafting or "implantable penis prosthesis" (16). Over the last decade, several new minimally invasive therapeutic modalities in the management of PD have included platelet-rich plasma (PRP), "hyaluronic acid (HA)," combination therapy of PRP and HA, "stem cell therapy (SCT)," "extracorporeal shockwave therapy (ESWT)," verapamil, steroids, interferon alfa-2b, and "mycophenolate mofetil (MMF)" (17). The general side effect is more with verapamil, steroids, and interferon alfa-2b, and the local "collagenase" adverse effects (18). In contrast, PRP shows a lower side effect, as no major side effect was reported in our study, as shown in Table (3).

Table (3) Comparison between many studies with different intra_lesional therapies for PD

	Hellstrom et al,28 2006(19)	Bennett et al, 2007(20)	Alessandro Zucchi et al,2016(21)	Our study
Number of patients	117	94	65	50
Intentional therapy	nterferon alfa2b	Verapamil	Hyaluronic acid	PRP
Dosage	× 106 U biweekly	10 mg every 2 wk	8 mg/wk	5 ml/ wk.
Injections times	6	6	10	8
Improvement in penile curvature (%)	27	18	37	43
Improvement in Erectile Dysfunction (%)	60	50	Not available	8
Decrease in plaque size, %	54.6	Not available	57	63

43% (22 patients) of our patients show improvement in penile curvature (decrease in degree of curvature from 35 degrees pretreatment to 19 degrees in subsequent follow-up), more than seen with interferon alfa-2, verapamil, and hyaluronic acid, as shown in table 3. 68% of our patients (34 patients) report significant improvements in sexual satisfaction (VAS scores) (pain through intercourse), and these results are comparable to those studies mentioned above. No major improvement in erectile dysfunction among our patients from pre- to post-treatment follow-up (8%); in contrast, we report improvement in ED (IIEF-5 score >21) in 60% and 50% with interferon alfa-2 and verapamil, respectively.

Conclusions

Efficacy of PRP as an intralesional treatment for patients with PD showed promising preliminary outcomes for the amelioration of plaque size, "penile curvature," and overall sexual satisfaction without the risk of local or general adverse effects, but it had a limited effect on the improvement of ED. It is better for this therapeutic modality to be initiated in the "early phase of the disease," as it is simple to perform and tolerable.

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